

AMENDMENT TO THE CLAIMS

Please amend the claims as follows:

1. (withdrawn) A method of modulating lysosomal function in a subject, comprising:
administering to the subject a therapeutically effective amount of a lysosomal modulating compound, a physiologically acceptable salt of the lysosomal modulating compound, or a combination thereof; wherein the lysosomal modulating compound comprises $M\text{-aa}_n\text{-CH=N=N}$, $M\text{-aa}_n\text{-CH}_2\text{-O-CO-[2-R-4-R-6-R-Phenyl]}$ (wherein each R is independently selected), $M\text{-aa}_n\text{-NH-CH}_2\text{-CH=N-NH-CO-NH}_2$, or $M\text{-N=N-CO-CH}_2\text{-aa}_n\text{-O-R}$, wherein;

M comprises H, benzyloxycarbonyl ("Z"), succinyl, methyloxysuccinyl, and butyloxycarbonyl;

aa comprises a blocked or unblocked amino acid with the L configuration, D configuration, or no chirality at the alpha-carbon, the amino acid selected from alanine, valine, leucine, isoleucine, proline, methionine, methionine sulfoxide, phenylalanine, tryptophan, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, phenylglycine, beta-alanine, norleucine, norvaline, alpha-aminobutyric acid, epsilon-aminocaproic acid, citrulline, hydroxyproline, homoarginine, ornithine, sarcosine, indoline 2-carboxylic acid, 2-azetidinecarboxylic acid, pipercolinic acid (2-piperidine carboxylic acid), O-methylserine, O-ethylserine, S-methylcysteine, S-ethylcysteine, S-benzylcysteine, $\text{NH}_2\text{-CH(CH}_2\text{-CH}_2\text{Et}_2\text{)-COOH}$, alpha-aminoheptanoic acid, $\text{NH}_2\text{-CH(CH}_2\text{-1-naphthyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-2-naphthyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclohexyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclopentyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclobutyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclopropyl)-COOH}$, trifluoroleucine, hexafluoroleucine, phenylalanine with its phenyl mono-, di-, or trisubstituted with K, alanine with its methyl side chain replaced with a lower alkyl side chain, alanine with its methyl side chain replaced with a lower alkyl group with an attached phenyl group, alanine with its methyl side chain replaced with a lower alkyl group with two attached phenyl groups, alanine with its methyl side chain replaced with a lower alkyl group with an attached phenyl group substituted with K, and alanine with

its methyl side chain replaced with a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K; n comprises an integer from 1 to about 20;

R comprises H, a lower alkyl group, a lower fluoroalkyl group, benzyl, a lower alkyl group substituted with J, a lower fluoroalkyl group substituted with J, 1-adamantly, 9-fluorenyl, phenyl, phenyl substituted with K, phenyl disubstituted with K, phenyl trisubstituted with K, naphthyl, naphthyl substituted with K, naphthyl disubstituted with K, naphthyl trisubstituted with K, a lower alkyl group with an attached phenyl group, a lower alkyl group with two attached phenyl groups, a lower alkyl group with an attached phenyl group substituted with K, or a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K;

J comprises halogen, COOH, OH, CN, NO₂, NH₂, lower alkyl-OH, lower alkoxy, lower alkylamine, di-lower alkylamine, lower alkoxy-CO-, lower alkyl-O-CO-NH, and lower alkyl-S; and

K comprises halogen, lower alkyl, lower alkyl-OH, lower perfluoroalkyl, lower alkoxy, NO₂, CN, OH, CO-OH, amino, lower alkylamine, C2-12 dialkylamine, lower acyl-O-CO-NH, lower alkoxy-CO-, and lower alkyl-S.

2. (withdrawn) The method of claim 1, wherein the lysosomal modulating compound comprises benzyloxycarbonyl-Phe-Ala-diazomethylketone, benzyloxycarbonyl-Phe-Phe-diazomethylketone, benzyloxycarbonyl-Phe-Lys-2,4,6-trimethylbenzoyloxymethylketone, benzyloxycarbonyl-Lys- diazomethylketone, H-Gly-Phe-Gly-aldehyde semicarbazone, diazoacetyl-DL-2-aminohexanoic acid-methyl ester, a physiologically acceptable salt thereof, or a combination thereof.
3. (withdrawn) The method of claim 1, wherein the lysosomal modulating compound comprises benzyloxycarbonyl-Phe-Ala-diazomethylketone.
4. (withdrawn) The method of claim 1, wherein the lysosomal modulating compound is a selective antagonist for at least one cathepsin enzyme.

5. (withdrawn) The method of claim 1, wherein n comprises an integer from 1 to 4.
6. (withdrawn) A method of modulating lysosomal function in a subject, comprising:
administering to the subject a therapeutically effective amount of a lysosomal modulating compound selected from peptidyl diazomethylketones, peptidyl semicarbazones, diazoacetyl peptidyl alkyl esters, and physiologically acceptable salts thereof.
7. (withdrawn) A method of reducing the risk of neurodegeneration in a subject, comprising:
administering to the subject a therapeutically effective amount of a lysosomal modulating compound, a physiologically acceptable salt of the lysosomal modulating compound, or a combination thereof, wherein enzymatic capacity of lysosomes in the subject is enhanced.
8. (withdrawn) The method of claim 7, wherein the lysosomal modulating compound comprises $M\text{-aa}_n\text{-CH=N=N}$; $M\text{-aa}_n\text{-CH}_2\text{-O-CO-[2-R-4-R-6-R-Phenyl]}$ (wherein each R is independently selected); $M\text{-aa}_n\text{-NH-CH}_2\text{-CH=N-NH-CO-NH}_2$; or $M\text{-N=N-CO-CH}_2\text{-aa}_n\text{-O-R}$, wherein;
M comprises H, benzyloxycarbonyl ("Z"), succinyl, methyloxysuccinyl, and butyloxycarbonyl;
aa comprises a blocked or unblocked amino acid with the L configuration, D configuration, or no chirality at the alpha-carbon, the amino acid selected from alanine, valine, leucine, isoleucine, proline, methionine, methionine sulfoxide, phenylalanine, tryptophan, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, phenylglycine, beta-alanine, norleucine, norvaline, alpha-aminobutyric acid, epsilon-aminocaproic acid, citrulline, hydroxyproline, homoarginine, ornithine, sarcosine, indoline 2-carboxylic acid, 2-azetidinedicarboxylic acid, pipercolinic acid (2-piperidine carboxylic acid), O-methylserine,

O-ethylserine, S-methylcysteine, S-ethylcysteine, S-benzylcysteine, $\text{NH}_2\text{-CH}(\text{CH}_2\text{-CHEt}_2\text{)-COOH}$, α -aminoheptanoic acid, $\text{NH}_2\text{-CH}(\text{CH}_2\text{-1-naphthyl)-COOH}$, $\text{NH}_2\text{-CH}(\text{CH}_2\text{-2-naphthyl)-COOH}$, $\text{NH}_2\text{-CH}(\text{CH}_2\text{-cyclohexyl)-COOH}$, $\text{NH}_2\text{-CH}(\text{CH}_2\text{-cyclopentyl)-COOH}$, $\text{NH}_2\text{-CH}(\text{CH}_2\text{-cyclobutyl)-COOH}$, $\text{NH}_2\text{-CH}(\text{CH}_2\text{-cyclopropyl)-COOH}$, trifluoroleucine, hexafluoroleucine, phenylalanine with its phenyl mono-, di-, or trisubstituted with K, alanine with its methyl side chain replaced with a lower alkyl side chain, alanine with its methyl side chain replaced with a lower alkyl group with an attached phenyl group, alanine with its methyl side chain replaced with a lower alkyl group with two attached phenyl groups, alanine with its methyl side chain replaced with a lower alkyl group with an attached phenyl group substituted with K, and alanine with its methyl side chain replaced with a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K;

n comprises an integer from 1 to about 20;

R comprises H, a lower alkyl group, a lower fluoroalkyl group, benzyl, a lower alkyl group substituted with J, a lower fluoroalkyl group substituted with J, 1-adamantyl, 9-fluorenyl, phenyl, phenyl substituted with K, phenyl disubstituted with K, phenyl trisubstituted with K, naphthyl, naphthyl substituted with K, naphthyl disubstituted with K, naphthyl trisubstituted with K, a lower alkyl group with an attached phenyl group, a lower alkyl group with two attached phenyl groups, a lower alkyl group with an attached phenyl group substituted with K, or a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K;

J comprises halogen, COOH , OH , CN , NO_2 , NH_2 , lower alkyl- OH , lower alkoxy, lower alkylamine, di-lower alkylamine, lower alkoxy- CO- , lower alkyl- O-CO-NH , and lower alkyl- S- ; and

K comprises halogen, lower alkyl, lower alkyl- OH , lower perfluoroalkyl, lower alkoxy, NO_2 , CN , OH , CO-OH , amino, lower alkylamine, C2-12 dialkylamine, lower acyl- O-CO-NH , lower alkoxy- CO- , and lower alkyl- S .

9. (presently amended) A method for treating neurodegeneration in a subject suffering from at least one of Alzheimer's disease, Parkinson's disease or lysosomal storage disorders, comprising:

administering to the subject a therapeutically effective amount of a lysosomal modulating compound, a physiologically acceptable salt of the lysosomal modulating compound or a combination thereof, wherein enzymatic capacity of lysosomes in the subject is enhanced.

10. (original) The method of claim 9, wherein the enhanced enzymatic capacity is sufficient to suppress neuropathogenesis.

11. (original) The method of claim 9, wherein the lysosomal modulating compound comprises M-aa_n-CH=N=N; M-aa_n-CH₂-O-CO-[2-R-4-R-6-R-Phenyl] (wherein each R is independently selected); M-aa_n-NH-CH₂-CH=N-NH-CO-NH₂; M-N=N-CO-CH₂-aa_n-O-R; wherein;

M comprises H, benzyloxycarbonyl ("Z"), succinyl, methyloxysuccinyl, and butyloxycarbonyl;

aa comprises a blocked or unblocked amino acid with the L configuration, D configuration, or no chirality at the alpha-carbon, the amino acid selected from alanine, valine, leucine, isoleucine, proline, methionine, methionine sulfoxide, phenylalanine, tryptophan, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, phenylglycine, beta-alanine, norleucine, norvaline, alpha-aminobutyric acid, epsilon-aminocaproic acid, citrulline, hydroxyproline, homoarginine, ornithine, sarcosine, indoline 2-carboxylic acid, 2-azetidinecarboxylic acid, pipercolinic acid (2-piperidine carboxylic acid), O-methylserine, O-ethylserine, S-methylcysteine, S-ethylcysteine, S-benzylcysteine, NH₂-CH(CH₂-CH₂-CH₂-COOH), alpha-aminoheptanoic acid, NH₂-CH(CH₂-1-naphthyl)-COOH, NH₂-CH(CH₂-2-naphthyl)-COOH, NH₂-CH(CH₂-cyclohexyl)-COOH, NH₂-CH(CH₂-cyclopentyl)-COOH, NH₂-CH(CH₂-cyclobutyl)-COOH, NH₂-CH(CH₂-cyclopropyl)-COOH, trifluoroleucine, hexafluoroleucine, phenylalanine with its phenyl mono-, di-, or

trisubstituted with K, alanine with its methyl side chain replaced with a lower alkyl side chain, alanine with its methyl side chain replaced with a lower alkyl group with an attached phenyl group, alanine with its methyl side chain replaced with a lower alkyl group with two attached phenyl groups, alanine with its methyl side chain replaced with a lower alkyl group with an attached phenyl group substituted with K, and alanine with its methyl side chain replaced with a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K;

n comprises an integer from 1 to about 20;

R comprises H, a lower alkyl group, a lower fluoroalkyl group, benzyl, a lower alkyl group substituted with J, a lower fluoroalkyl group substituted with J, 1-adamantyl, 9-fluorenyl, phenyl, phenyl substituted with K, phenyl disubstituted with K, phenyl trisubstituted with K, naphthyl, naphthyl substituted with K, naphthyl disubstituted with K, naphthyl trisubstituted with K, a lower alkyl group with an attached phenyl group, a lower alkyl group with two attached phenyl groups, a lower alkyl group with an attached phenyl group substituted with K, or a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K;

J comprises halogen, COOH, OH, CN, NO₂, NH₂, lower alkyl-OH, lower alkoxy, lower alkylamine, di-lower alkylamine, lower alkoxy-CO-, lower alkyl-O-CO-NH, and lower alkyl-S; and

K comprises halogen, lower alkyl, lower alkyl-OH, lower perfluoroalkyl, lower alkoxy, NO₂, CN, OH, CO-OH, amino, lower alkylamine, C2-12 dialkylamine, lower acyl-O-CO-NH, lower alkoxy-CO-, and lower alkyl-S.

12. (original) The method of claim 9, wherein the lysosome modulating compound comprises at least one of benzyloxycarbonyl-Phe-Ala-diazomethylketone, benzyloxycarbonyl-Phe-Phe-diazomethylketone, benzyloxycarbonyl-Phe-Lys-2,4,6-trimethylbenzoyloxymethylketone, benzyloxycarbonyl-Lys- diazomethylketone, H-Gly-Phe-Gly-aldehyde semicarbazone, diazoacetyl-DL-2-aminohexanoic acid-methyl ester or physiologically acceptable salts thereof.

13. (original) The method of claim 9, wherein the compound comprises benzyloxycarbonyl-Phe-Ala-diazomethylketone or physiologically acceptable salts thereof.

14. (original) The method of claim 9, wherein the compound is a selective antagonist for at least one cathepsin enzyme.

15. (withdrawn) A pharmaceutical preparation, including:

at least one lysosomal modulating compound, a physiologically acceptable salt of the lysosomal modulating compound, or a combination thereof; wherein the lysosomal modulating compound comprises $M\text{-aa}_n\text{-CH=N=N}$; $M\text{-aa}_n\text{-CH}_2\text{-O-CO-[2-R-4-R-6-R-Phenyl]}$ (wherein each R is independently selected); $M\text{-aa}_n\text{-NH-CH}_2\text{-CH=N-NH-CO-NH}_2$; $M\text{-N=N-CO-CH}_2\text{-aa}_n\text{-O-R}$, wherein;

M comprises H, benzyloxycarbonyl ("Z"), succinyl, methyloxysuccinyl, and butyloxycarbonyl;

aa comprises a blocked or unblocked amino acid with the L configuration, D configuration, or no chirality at the alpha-carbon, the amino acid selected from alanine, valine, leucine, isoleucine, proline, methionine, methionine sulfoxide, phenylalanine, tryptophan, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, phenylglycine, beta-alanine, norleucine, norvaline, alpha-aminobutyric acid, epsilon-aminocaproic acid, citrulline, hydroxyproline, homoarginine, ornithine, sarcosine, indoline 2-carboxylic acid, 2-azetidinecarboxylic acid, pipercolinic acid (2-piperidine carboxylic acid), O-methylserine, O-ethylserine, S-methylcysteine, S-ethylcysteine, S-benzylcysteine, $\text{NH}_2\text{-CH(CH}_2\text{-CH}_2\text{Et}_2\text{)-COOH}$, alpha-aminoheptanoic acid, $\text{NH}_2\text{-CH(CH}_2\text{-1-naphthyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-2-naphthyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclohexyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclopentyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclobutyl)-COOH}$, $\text{NH}_2\text{-CH(CH}_2\text{-cyclopropyl)-COOH}$, trifluoroleucine, hexafluoroleucine, phenylalanine with its phenyl mono-, di-, or trisubstituted with K, alanine with its methyl side chain replaced with a lower alkyl side chain, alanine with its methyl side chain replaced with a lower alkyl group with an

attached phenyl group, alanine with its methyl side chain replaced with a lower alkyl group with two attached phenyl groups, alanine with its methyl side chain replaced with a lower alkyl group with an attached phenyl group substituted with K, and alanine with its methyl side chain replaced with a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K;

n comprises an integer from 1 to about 20;

R comprises H, a lower alkyl group, a lower fluoroalkyl group, benzyl, a lower alkyl group substituted with J, a lower fluoroalkyl group substituted with J, 1-adamantyl, 9-fluorenyl, phenyl, phenyl substituted with K, phenyl disubstituted with K, phenyl trisubstituted with K, naphthyl, naphthyl substituted with K, naphthyl disubstituted with K, naphthyl trisubstituted with K, a lower alkyl group with an attached phenyl group, a lower alkyl group with two attached phenyl groups, a lower alkyl group with an attached phenyl group substituted with K, or a lower alkyl group with two attached phenyl groups and at least one phenyl group substituted with K;

J comprises halogen, COOH, OH, CN, NO₂, NH₂, lower alkyl-OH, lower alkoxy, lower alkylamine, di-lower alkylamine, lower alkoxy-CO-, lower alkyl-O-CO-NH, and lower alkyl-S-; and

K comprises halogen, lower alkyl, lower alkyl-OH, lower perfluoroalkyl, lower alkoxy, NO₂, CN, OH, CO-OH, amino, lower alkylamine, C2-12 dialkylamine, lower acyl-O-CO-NH, lower alkoxy-CO-, and lower alkyl-S-.

16. (withdrawn) The pharmaceutical preparation of claim 15, wherein the compound is administered to a subject at a therapeutically effective amount to modulate cellular content of lysosomes.

17. (withdrawn) The pharmaceutical preparation of claim 15, wherein the compound comprises at least one of benzyloxycarbonyl-Phe-Ala-diazomethylketone, benzyloxycarbonyl-Phe-Phe-diazomethylketone, benzyloxycarbonyl-Phe-Lys-2,4,6-trimethylbenzoyloxymethylketone, benzyloxycarbonyl-Lys- diazomethylketone, H-Gly-

Phe-Gly-aldehyde semicarbazone, diazoacetyl-DL-2-aminohexanoic acid-methyl ester, or physiologically acceptable salts thereof.

18. (withdrawn) The pharmaceutical preparation of claim 15, wherein the compound comprises benzyloxycarbonyl-Phe-Ala-diazomethylketone or physiologically acceptable salts thereof.

19. (withdrawn) The pharmaceutical preparation of claim 15, wherein the compound is a selective antagonist for at least one cathepsin enzyme.

Cancel claims 20-23 without prejudice.

24. (new) The method of claim 9 wherein the therapeutically effective amount of a lysosomal modulating compound, a physiologically acceptable salt of the lysosomal modulating compound or a combination thereof administered to the subject is sufficient to enhance enzymatic capacity of lysosomes but is not sufficient to generate pathogenic accumulations of proteins or protein fragments.